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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/977,221	11/24/97	STRACKE M	2026-4149US3

HM12/0209

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EXAMINER	
LONGTON, E	

ART UNIT	PAPER NUMBER
1652	7

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 08/977,221	Applicant(s) Stracke et al.
	Examiner Enrique D. Longton	Group Art Unit 1652

☒ Responsive to communication(s) filed on *Nov 16, 1998* .

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), ~~or thirty days~~, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *3-6, 9, 11, 12, and 16-19* is/are pending in the application.

Of the above, claim(s) *9* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *3-6, 11, 12, and 16-19* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *3*

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1652.

The drawings are objected to because of the defects noted on Form PTO 948. Correction is required.

Status of the Claims

Applicant's election with traverse of claims 3-6, 11, 12 and 16-19 in Paper No. 6, filed 11/16/98, is acknowledged. Applicants' traversal is not found persuasive because no reasons or arguments have been given for the traversal. Claims 1, 2, 7, 8, 10 and 13-15 have been canceled by Applicants. Claim 9 is withdrawn from further consideration by the Examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

The requirement is still deemed proper and is therefore made FINAL.

Information Disclosure Statement

A signed and initialed copy of form PTO-1449 is enclosed with this office action. Applicant should note that those references not initialed on Applicant's PTO-1449 were not considered because Examiner is unable to locate them in the instant application or in the parent

applications. Applicant is requested to provide copies of these references for consideration as well as the dates of publication for the indicated references on pages 6 and 7 of Form PTO-1449.

Objections to the Specification

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821(d). Applicant is reminded that sequence(s) disclosed in the specification must be identified by SEQ ID NO(s). Specifically, Figure 18 contains amino acid sequences not identified by SEQ ID NO in the Brief Description of the figure and pages 38 and 39 contain sequences not identified by SEQ ID NO. Correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3, 5, 11, 12, 16, 17, 18 and 19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a naturally-occurring human autotaxin from melanoma cells and peptides derived therefrom, does not reasonably provide enablement for any autotaxin from any source, mutant, species homologue or variant thereof. The specification does

not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure would require undue experimentation are summarized in Ex parte Forman (230 USPQ 546 (Bd. Pat. App. & Int. 1986)). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Claims 3, 5, 11, 12, 16, 17, 18 and 19 are directed to isolated polypeptides "corresponding to" autotaxin from any source and encompass mutants, species homologues, variants thereof and a method of purifying the polypeptide. The specification has only disclosed an isolated naturally-occurring autotaxin from human melanoma cells, as well as peptides derived from this protein. It would require undue experimentation for a person having ordinary skill in the art at the time the invention was made to be able to isolate, identify or purify proteins "corresponding to" autotaxin from any other source, including mutants, species homologues and variants thereof, such that the skilled artisan could make and use the invention commensurate with the scope of the claims. Applicants have only provided guidance for the isolation and purification of a protein termed autotaxin, isolated from human melanoma cells, yet the claims are not limited in any way as to the source of the claimed protein, its activity (except claim 19), or to any means of synthesizing a protein "corresponding to" autotaxin. No link has been provided between the single disclosed,

naturally-occurring autotaxin, and any other protein, or mutant or variant thereof. The state of the prior art as it relates to the prediction of protein structure/function relationships and protein purification is such that correlations between structure and function are *a priori* highly unpredictable. Given this lack of predictability and the breadth of the claims, in view of the single autotaxin protein disclosed from human melanoma cells, it would require undue experimentation for a person having ordinary skill in the art to be able to practice the claimed invention in a manner reasonably correlated with the scope of the claims. Limiting the claims to the naturally-occurring autotaxin isolated from human melanoma cells and the peptides derived therefrom, would overcome this portion of the rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3, 5, 16 and 17 are rejected under 35 U.S.C. § 112, second paragraph, for failing to distinctly claim the subject matter which Applicant regards as his invention.

Claims 3, 5, 16 and 17 are directed to an isolated polypeptide "corresponding to" autotaxin yet no indication has been made in the specification to define what is meant by the term "corresponding to". How many amino acids does a protein have to have in common with the disclosed autotaxin to "correspond to" it? What activity does such a protein have to possess such that it would fit within the set of all proteins "corresponding to" autotaxin? Without a clear

definition of what is meant by the term "corresponding to" the metes and bounds of the claimed invention are unclear and confusing.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 3, 16 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Buckley *et al.* (1990). The claims are directed to a polypeptide comprising a fragment of autotaxin having at least 5 amino acids. The reference teaches a protein which comprises 15 amino acids of SEQ ID NO:34 (Figure 3), as evidenced by the associated database submission and sequence alignment (see the alignment of SEQ ID NO:34 with Accession No. A39216). Barring evidence to the contrary, the recombinantly produced protein would be no different from the protein disclosed by the reference. Since SEQ ID NO:34 is a peptide corresponding to autotaxin and the reference teaches a sequence comprising 15 amino acids of SEQ ID NO:34, the claims are anticipated by the reference.

Claims 3, 16 and 18 are rejected under 35 U.S.C. 102(a) as being anticipated by Oda *et al.* (1991). The claims are directed to a polypeptide comprising a fragment of autotaxin having at least 5 amino acids. The reference teaches a protein which comprises 12 amino acids of SEQ ID NO:36 (Table 1), as evidenced by the associated database submission and sequence alignment (see the alignment of SEQ ID NO:36 with Accession No. A41179). Barring evidence to the contrary, the recombinantly produced protein would be no different from the protein disclosed by the reference. Since SEQ ID NO:36 is a peptide corresponding to autotaxin and the reference teaches a sequence comprising 12 amino acids of SEQ ID NO:36, the claims are anticipated by the reference.

Claims 3, 16 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Culp *et al.* (1985). The claims are directed to a polypeptide comprising a fragment of autotaxin having at least 5 amino acids. The reference teaches a protein which comprises 10 amino acids of SEQ ID NO:69 (Figure 3), as evidenced by the associated database submission and sequence alignment (see the alignment of SEQ ID NO:69 with Accession No. A25274). Barring evidence to the contrary, the recombinantly produced protein would be no different from the protein disclosed by the reference. Since SEQ ID NO:69 is a peptide corresponding to autotaxin and the reference teaches a sequence comprising 10 amino acids of SEQ ID NO:69, the claims are anticipated by the reference.

Claims 3, 4, 16 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Lawrence *et al.* (1990). The claims are directed to a polypeptide comprising SEQ ID NO:1 or a protein comprising an amino acid sequence corresponding to autotaxin having at least 5 amino acids. The reference teaches a protein which comprises all of SEQ ID NO:1 (figure 2), as evidenced by the associated database submission and sequence alignment (see the alignment of SEQ ID NO:1 with Accession No. Q69545). Barring evidence to the contrary, the recombinantly produced protein would be no different from the protein disclosed by the reference. Since SEQ ID NO:1 is a peptide corresponding to autotaxin and the reference teaches a sequence comprising all of SEQ ID NO:1, the claims are anticipated by the reference.

Claims 3, 4, 16 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Zierer *et al.* (1990). The claims are directed to a polypeptide comprising SEQ ID NO:3 or a protein comprising an amino acid sequence corresponding to autotaxin having at least 5 amino acids. The reference teaches a protein which comprises all of SEQ ID NO:3 (figure 2), as evidenced by the associated database submission and sequence alignment (see the alignment of SEQ ID NO:3 with Accession No. S12888). Barring evidence to the contrary, the recombinantly produced protein would be no different from the protein disclosed by the reference. Since SEQ ID NO:3 is a peptide corresponding to autotaxin and the reference teaches a sequence comprising all of SEQ ID NO:3, the claims are anticipated by the reference.

Claims 3, 4, 16 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Henderson *et al.* (1989). The claims are directed to a polypeptide comprising SEQ ID NO:4 or a protein comprising an amino acid sequence corresponding to autotaxin having at least 5 amino acids. The reference teaches a protein which comprises all of SEQ ID NO:4 (figure 1), as evidenced by the associated database submission and sequence alignment (see the alignment of SEQ ID NO:4 with Accession No. S06727). Barring evidence to the contrary, the recombinantly produced protein would be no different from the protein disclosed by the reference. Since SEQ ID NO:4 is a peptide corresponding to autotaxin and the reference teaches a sequence comprising all of SEQ ID NO:4, the claims are anticipated by the reference.

Claims 3, 4, 16 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Stainthorpe *et al.* (1990). The claims are directed to a polypeptide comprising SEQ ID NO:27 or a protein comprising an amino acid sequence corresponding to autotaxin having at least 5 amino acids. The reference teaches a protein which comprises all of SEQ ID NO:27 (figure 3), as evidenced by the associated database submission and sequence alignment (see the alignment of SEQ ID NO:27 with Accession No. JQ0700). Barring evidence to the contrary, the recombinantly produced protein would be no different from the protein disclosed by the reference. Since SEQ ID NO:27 is a peptide corresponding to autotaxin and the reference teaches a sequence comprising all of SEQ ID NO:27, the claims are anticipated by the reference.

Claims 3, 4, 16 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Knight *et al.* (1990). The claims are directed to a polypeptide comprising SEQ ID NO:28 or a protein comprising an amino acid sequence corresponding to autotaxin having at least 5 amino acids. The reference teaches a protein which comprises all of SEQ ID NO:28 (figure 15), as evidenced by the associated database submission and sequence alignment (see the alignment of SEQ ID NO:28 with Reference No. TN024561). Barring evidence to the contrary, the recombinantly produced protein would be no different from the protein disclosed by the reference. Since SEQ ID NO:28 is a peptide corresponding to autotaxin and the reference teaches a sequence comprising all of SEQ ID NO:28, the claims are anticipated by the reference.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 5, 6 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Buckley *et al.* (1990), Oda *et al.* (1991), Culp *et al.* (1985), Lawrence *et al.* (1990), Zierer *et al.* (1990), Stainthorpe *et al.* (1990) and Knight *et al.* (1989) in view of US Patent 5,003,047, to Yarmush *et al.* filed 1/10/89.

The primary references are directed to proteins comprising fragments of autotaxin at least 5 amino acids in length as well as proteins comprising specific SEQ ID NOs corresponding to autotaxin (see each of the rejections under 35 USC 102). The primary references do not teach the polypeptides bound to a solid support. The secondary reference, US Patent 5,003,047 to Yarmush *et al.* is directed to a method for purifying a biologically active ligate including the step of covalently binding a ligand to a solid support (claim 1; paragraph spanning columns 1-2; column 4, lines 24-31). It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to use the polypeptides disclosed in each of the primary references in combination with the known method of immobilizing a ligand to a solid support to arrive at the claimed invention. A person having ordinary skill in the art would have recognized that by immobilizing the proteins of the prior art to solid supports, a powerful assay technique for the identification of receptors or other specific ligands to the immobilized proteins might be developed. Such a person would be motivated to do this because each of the polypeptides of the primary references is a biologically important molecule, the identification of specific receptors therefor, would be expected to lead to the isolation and purification of potentially new and pharmaceutically useful proteins. The person having ordinary skill in the art would have had a reasonable expectation of success in view of the nature of biospecific ligand/receptor interactions and the success of methods such as that of the '047 patent which are routinely used in ligand binding studies. Therefore, the claims are obvious over the cited references.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 3-6, 11, 12 and 16-19 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. 5,449,753 in view of US Patent 5,003,047 to Yarmush *et al.* (filed January 10, 1989). Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the instant application are directed to an autotaxin protein isolated from human melanoma cells, while the claims of the '753 patent are also directed to an autotaxin protein isolated from human melanoma cells. The '753 patent does not claim the polypeptide bound to a solid support. The secondary reference, US Patent 5,003,047 to Yarmush *et al.* is directed to a method for purifying a biologically active ligate including the step of covalently binding a ligand to a solid support (claim 1; paragraph spanning columns 1-2; column 4, lines 24-31). It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to use the polypeptides claimed in the '753 patent in combination with the known method of

immobilizing a ligand to a solid support to arrive at the claimed invention. A person having ordinary skill in the art would have recognized that by immobilizing the protein claimed in the '753 patent to a solid support, a powerful assay technique for the identification of receptors or other specific ligands to the immobilized protein might be developed. Such a person would be motivated to do this because the claimed autotaxin of the '753 patent is a biologically important molecule and the identification of specific receptors therefor would be expected to lead to the isolation and purification of potentially new and pharmaceutically useful proteins. The person having ordinary skill in the art would have had a reasonable expectation of success in view of the nature of biospecific ligand/receptor interactions and the success of methods such as that of the '047 patent which are routinely used in ligand binding studies. Furthermore, the claimed method of purification of autotaxin from human A2058 melanoma cells (claims 11 and 12) would have been *prima facie* obvious to the skilled artisan at the time the invention was made given the fact that the '753 patent claims autotaxin isolated from human melanoma cells (claim 2). Column chromatographic techniques and salt fractionation of protein solutions are well-known and established protein purification techniques and would have been well within the purview of a person having ordinary skill in the art at the time the invention was made. Motivation to purify the autotaxin protein from human melanoma cells is provided by claim 2 of the '753 patent which discloses that autotaxin is isolated from these cells. The skilled artisan would have recognized that a protein such as autotaxin which is associated with cell motility (claim 1, '753 patent) would have been a potentially important protein to isolate for its potential use in anticancer therapeutics.

The skilled artisan would have had a reasonable expectation of success in light of the well-established techniques of column chromatography and salt-fractionation applied to protein purification procedures. Therefore, the claims are obvious over the cited references.

Inquiries

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Enrique D. Longton whose telephone number is (703) 305-4062. The Examiner can normally be reached from 7:45 a.m. to 4:15 p.m. on weekdays. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Robert A. Wax, can be reached at (703) 308-4216. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Fax Center number is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Enrique D. Longton, Ph.D.
February 1, 1999